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EXAMINER	
PAK, YONG D	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,507	SPANGENBERG ET AL.	
	Examiner	Art Unit	
	YONG D. PAK	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *Claims 30-31, 33, 35, 40-45, 49-54, 56, and 58-71* is/are pending in the application.

4a) Of the above claim(s) *43-45,49-54,56 and 64-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30,31,33,35,40-42 and 58-63* is/are rejected.

7)☐ Claim(s) ____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 of PCT/AU04/00493.

The amendment filed on February 24, 2010, amending claims 30-31, 33, 40-41, 58, and 60-63, has been entered. No new matter has been entered.

Claims 30-31, 33, 35, 40-45, 49-54, 56, and 58-71 are pending. Claims 43-45, 49-54, 56, and 64-71 are withdrawn. Claims 30-31, 33, 35, 40-42, and 58-63 are under consideration.

A Supplement Final Rejection is issued herewith to correct claim numberings in the rejections under 112, 1st paragraph.

Election/Restrictions

Applicants elected with traverse Group I (claims 30-42) with an election of SEQ ID NO:271 in the reply filed on September 25, 2008 is. Applicants argue that claims 64-71 do not lack a special technical feature with group I because claims 64-71 are directed in part to the subject matter (polynucleotide encoding MDH or polynucleotide encoding MDH of SEQ ID NO:271 or variants thereof) that falls within group I. This is not found persuasive because the main claim, claim 64, is not necessarily drawn to a construct comprising a polynucleotide encoding MDH. If claims of Group I are found allowable, claims 65-70 maybe eligible for rejoinder if claims 65-70 require all the limitations of the allowable product. Therefore, in order to retain the right to rejoinder, applicant is advised that the claims to the nonelected invention(s) should be amended

during prosecution to require the limitations of the elected invention. **Failure to do so may result in a loss of the right to rejoinder.**

The requirement is still deemed proper and is therefore made FINAL.

Claims 42, 59, and 63 are partially directed to non-elected inventions (plant, plant seed or other plant part). For examination purposes, the Examiner will only examine the elected invention, a plant cell comprising a construct.

Response to Arguments

Applicant's amendment and arguments filed on February 24, 2010, have been fully considered and are deemed to be persuasive to overcome some of the objections/rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

In view of the amendment of claims 30-31, 40-41, 58, and 60-62, the objections to claims 30-31, 40-41, 58, and 60-62 have been **withdrawn.**

Claims 35, 42, 59, and 63 are objected to because of the following informalities:

Claims 35, 42, 59, and 63 are objected for the recitation of "a nucleic acid or nucleic acid fragment according to claim 30", "a construct according claim 35", of "a nucleic acid or nucleic acid fragment according to claim 58", and "a construct according

claim 62", respectively. Since the nucleic acids and constructs are dependent claims, it is suggested that the claims be amended “the nucleic acid” or “the construct”, for example.

Appropriate correction is required.

Applicants argue that claims 35 and 42 are not dependent claims. Examiner respectfully disagrees. Claim 35 depends from claim 30 and claim 42 depends from claim 35.

Hence the objection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Withdrawn Rejections

In view of the amendment of claim 30 (deletion of the phrase “MDH-like polypeptide”), the rejection of claim 30 and claims 31, 35, 40-42, 58-59, and 61-63 depending therefrom under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been **withdrawn**.

In view of the amendment of claim 30 (deletion of the phrase “functionally active”), the rejection of claim 30 and claims 31, 35, 40-42, 58-59, and 61-63 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and

distinctly claim the subject matter which applicant regards as the invention has been **withdrawn**.

In view of the amendment of claim 33 (deletion of the phrase “shown in”), the rejection of claim 33 and claim 60 depending therefrom under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been **withdrawn**.

New Rejection

Claims 31 and claims 35 and claims 40-42, 58-59, and 61-63 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 recites the limitation "nucleic acid according to claim 30 wherein said nucleic acid or nucleic acid fragment" in lines 1-2. Claim 35 recites the limitation " a nucleic acid or nucleic acid fragment according to claim 30" in lines 1-2. There is insufficient antecedent basis for the above limitations in the claims because claim 30 does not recite a “nucleic acid fragment”.

Maintained Rejections

Claim 33 and claim 60 depending therefrom remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 33 recite the phrase "functionally active". The metes and bounds of the phrase in the context of the above claims are not clear to the Examiner. The phrase encompasses many different functions and activities, such as enzymatic activity and ability to illicit antibodies, which can be considered as "functionally active" and therefore is outside the scope of the invention. A perusal of the specification did not provide the Examiner with a specific definition for the above phrase. Therefore, it is not clear to the Examiner either from the specification or from the claim as to what specific activities/functions are encompassed in "functionally active". Examiner requests clarification of the above phrase. For examination purposes, the above phrase has been interpreted as polypeptides having any function or activity.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that the phrase "functionally active" is defined in the specification, pages 5-6. The specification defines the above phrase as "the fragment or variant has one or more of the biological properties of the proteins.. MDH, MDH-like..". The specification does not clarify what properties are encompassed in "biological properties". The phrase (functionally active/biological properties) encompasses many different biological functions and activities, such as enzymatic activity and ability to illicit antibodies, which can be considered as "functionally active" or

a "biological property" and therefore the phrase is outside the scope of the invention. Thus, it is not clear to the Examiner either from the specification or from the claim as to what specific activities/functions are encompassed in "functionally active".

Hence the rejection is **maintained**.

Claim 58 and claim 59 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 58 recites the phrase "shown in". The metes and bounds of the phrase in the context of the claims are not clear. It is not clear to the Examiner if the recited nucleic acid sequence has the nucleic acid sequence of SEQ ID NO: or is a representative member of a genus. Examiner suggests amending the phrase as "the nucleic acid sequence of SEQ ID NO:".

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that the rejection should be withdrawn because SEQ ID Nos. are referred to without the phrase "shown in". Examiner respectfully disagrees. Claim 58 recites the phrase "shown in".

Hence the rejection is **maintained**.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30-31, 33, 35, and 40-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to **(A)** polynucleotide encoding MDH polypeptide, from a clover (*Trifolium*); **(B)** polynucleotide of (A) which is from white clover (*T. repens*); and **(C)** polynucleotides that are functionally active variants having at least 95% sequence identity to SEQ ID NO:271; and **(D)** construct comprising said polynucleotide of (A), (B), or (C) and plant cell comprising said construct.

It is noted that MPEP 2111.01 states that "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." Regarding claim 33 (d), the examiner has broadly interpreted “functionally active" to encompass polypeptides having any function (see the rejection of the phrase “functionally active” under 35 USC 112, 2nd paragraph). Examiner has broadly interpreted claims 30-31, 33, 35, and 40-42 to encompass **(A)** a polynucleotide encoding (1) MDH isolated from any or all *Trifolium* sources, including any or all variants, mutants, or recombinants thereof; **(B)** a polynucleotide encoding MDH from white clover (*T. repens*), including any or all any variants, mutants, or recombinants of; **(C)** any or all polynucleotides having at least 95% sequence identity to SEQ ID NO:271 and encoding polypeptides having unknown

function; and **(D)** construct comprising said polynucleotide of (A), (B), or (C), and plant cell comprising said construct. Therefore, the claims are drawn to a genus comprising polynucleotides having unknown structure and/or unknown function.

In *University of Calfornia v. Eli Lilly & Co.,* 43 USPQZd 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, (or) chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

The recitation of "MDH" fails to provide a sufficient description of the claimed genus of proteins as it merely describes the functional features of the genus without providing any definition of the structural features of the species within the genus. The

CAFC in UC California v. Eli Lilly, (43 USPQ2d 1398) stated that: "in claims to genetic material, however a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus." Similarly with the claimed genus of polynucleotides encoding "erythrose reductase" proteins, the functional definition of the genus does not provide any structural information commonly possessed by members of the genus which distinguish the protein species within the genus from other proteins such that one can visualize or recognize the identity of the members of the genus.

The 30-31, 35, and 40-42 are drawn to polynucleotides having unknown structure, encompassing polynucleotides encoding mutants, recombinant, and variants of any or all polypeptides having MDH activity that are from any *Trifolium* species or *T. repens*. The specification only describes a polynucleotide of SEQ ID NO:271 encoding a polypeptide having MDH activity or the full complement of SEQ ID NO:271, vector comprising said polynucleotide, and a plant cell comprising said vector. While MPEP 2163 acknowledges that in certain situations "one species adequately supports a genus," it also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be

achieved by disclosing only one species within the genus." In view of the widely variant species encompassed by the genus, the one example is not enough and does not constitute a representative number of species to describe the whole genus of polynucleotides having unknown structure, and there is no evidence on the record of the relationship between the structure of the polynucleotide of SEQ ID NO:271 and the structure of any or all variants, recombinant and mutants of SEQ ID NO:271 or any or all MDH isolated from any *Trifolium* species or *T. repens*. Therefore, the specification fails to describe a representative species of the genus.

Claim 33 is drawn to many polynucleotides encoding functionally unrelated polypeptides encompassed within the scope of these clams, including partial sequences, resulting in a substantial variation within the genus. The genus of these polynucleotides comprises a large variable genus encompassing many different polynucleotides encoding polypeptides having different activity or no activity or unknown activity. The specification only describes a polynucleotide of SEQ ID NO:271 encoding a polypeptide having MDH activity or the full complement of SEQ ID NO:271, vector comprising said polynucleotide, and a plant cell comprising said vector. While MPEP 2163 acknowledges that in certain situations "one species adequately supports a genus," it also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." In view of the widely variant species encompassed by the genus, this one example is not enough and does not constitute a representative number of species to describe the whole genus of

polynucleotides encoding polypeptides having unknown structure and/or unknown function. The specification fails to describe additional representative species of the polynucleotides by any identifying characteristics or properties of the encoded polypeptides, for which no predictability of function is apparent. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 30-31, 33, 35, and 40-42.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that the claims meet written description because the specification discloses multiple MDH sequences from *Trifolium*. Examiner respectfully disagrees. The specification only discloses cDNA encoding a malate dehydrogenase from *Trifolium repens* and a cDNA encoding a malate dehydrogenase from *Lolium perenne*. The specification does not describe a method of isolating cDNA encoding non-*Trifolium repens* MDH proteins nor describe any structural features of *Trifolium repens* MDH cDNA that would have been expected to be shared by members of the

claimed genus. At the time of filing, cDNA encoding *Trifolium repens or Trifolium* MDH were not known in the art (see BRENDA Database EC 1.1.1.37 – cited previously on form PTO-892 mailed on May 26, 2010). Therefore, at the time of filing, the level of the knowledge and skill in the art did not allow those skilled in the art to structurally envisage or recognize cDNA encoding non- *Trifolium repens* MDH because it is known that corresponding genes/proteins in different species tend to differ in sequence and the amount and type of sequence variation is unpredictable. Because the structure of cDNA encoding *Trifolium* MDH would be expected to vary unpredictably from the structure of the single, described cDNA encoding the*Trifolium repens* MDH of SEQ ID NO:272, the disclosed *Trifolium repens* MDH cDNA of SEQ ID NO:271 is not a "representative number" of species within the claimed genus. Given this lack of additional representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.

Hence the rejection is **maintained.**

Claims 30-31, 33, 35, and 40-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide of SEQ ID NO:271 encoding a polypeptide having MDH activity or the full complement of SEQ ID NO:271, vector comprising said polynucleotide, and a plant cell comprising said vector, does not reasonably provide enablement for a polynucleotide having unknown

structure and/or unknown function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to **(A)** polynucleotide encoding MDH polypeptide, from a clover (*Trifolium*); **(B)** polynucleotide of (A) which is from white clover (*T. repens*); and **(C)** polynucleotides that are functionally active variants having at least 95% sequence identity to SEQ ID NO:271; and **(D)** construct comprising said polynucleotide of (A), (B), or (C) and plant cell comprising said construct.

The breadth of the claims.

It is noted that MPEP 2111.01 states that "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." Regarding claim 33 (d), the examiner has broadly interpreted “functionally active" to encompass polypeptides having any function (see the rejection of the phrase “functionally active” under 35 USC 112, 2nd paragraph). Examiner has broadly interpreted claims 30-31, 33, 35, and 40-42 to encompass **(A)** a polynucleotide encoding (1) MDH isolated from any or all *Trifolium*

sources, including any or all variants, mutants, or recombinants thereof; **(B)** a polynucleotide encoding MDH from white clover (*T. repens*), including any or all any variants, mutants, or recombinants of; **(C)** any or all polynucleotides having at least 95% sequence identity to SEQ ID NO:271 and encoding polypeptides having unknown function; and **(D)** construct comprising said polynucleotide of (A), (B), or (C), and plant cell comprising said construct

Therefore, the claims are drawn to polynucleotides having unknown structure and/or unknown function. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides of virtually any structure and/or function or polypeptides/variants having virtually any structure and/or function. In the instant case, the specification a polynucleotide of SEQ ID NO:271 encoding a polypeptide having MDH activity or the full complement of SEQ ID NO:271, vector comprising said polynucleotide, and a plant cell comprising said vector.

The quantity of experimentation required to practice the claimed invention based on the teachings of the specification.

While enzyme isolation techniques, recombinant and mutagenesis techniques were known in the art at the time of the invention, e.g. hybridization or mutagenesis, and it is routine in the art to screen for variants comprising multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within the encoded protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are

limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. Furthermore, while the skilled artisan can produce variants of the polynucleotide of SEQ ID NO:271 having the recited structural characteristics using well-known and widely used techniques in the art, the amount of experimentation required is not routine due to the fact that the number of species encompassed by the claims is extremely large.

In the absence of: (a) rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function and (b) a correlation between structure and MDH activity, the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. One of skill in the art would have to test these infinite possible polypeptides to determine (1) which ones have MDH activity, (2) the specific substrates targeted by such proteins and (3) how to use those polypeptides encompasses by the claims which do not have MDH activity. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, as is the case herein, the specification must provide a reasonable amount of guidance which respect to the direction in which the experimentation should proceed so that a reasonable number of species can be selected for testing. In view of the fact that such guidance has not been provided in the instant specification, it would require undue experimentation to enable the full scope of the claims.

The state of prior art, the relative skill of those in the art, and predictability or unpredictability of the art.

Since the amino acid sequence of the encoded protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. In the instant case, neither the specification or the art provide a correlation between structure and activity such that one of skill in the art can envision the structure of any polypeptides having the same biological function as that of the polypeptide encoded by SEQ ID NO:271 or predict the function of a polypeptide from its primary structure. In addition, the art does not provide any teaching or guidance as to (1) which amino acids within the polypeptides encoded by SEQ ID NO: 271 or MDH can be modified and which ones are conserved such that one of skill in the art can make the recited polynucleotides encoding polypeptides having the same enzymatic activity as that of the polypeptide encoded by SEQ ID NO:271, (2) which segments of the polypeptide encoded by SEQ ID NO:271 or MDH are essential for activity, and (3) the general tolerance of MDH proteins to structural modifications and the extent of such tolerance. The art clearly teaches that changes in a protein's amino acid sequence to obtain the desired activity without any guidance/knowledge as to which amino acids in a protein are required for that activity is highly unpredictable. At the time of the invention there

was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity. For example, Branden et al. (Introduction to Protein Structure, Garland Publishing Inc., New York, page 247, 1991 – cited previously on form PTO-892 mailed on March 30, 2009) teach that (1) protein engineers are frequently surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes, (2) the often surprising results obtained by experiments where single mutations are made reveal how little is known about the rules of protein stability, and (3) the difficulties in designing de novo stable proteins with specific functions.

Further regarding claim 33, the function of a polypeptide cannot be predicted from its structure and the specification does not teach how to use polypeptides having any function or having no activity. The quantity of experimentation in this area is extremely large since there is significant variability in the activity of the polynucleotides in the claims. It would require significant study to identify the actual function of the encoded polypeptides and identifying a use for the encoded polypeptide would be an inventive, unpredictable and difficult undertaking. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Further, the art is extremely unpredictable with regard to protein function in the absence of realizable information regarding its activity. Even very similar proteins may have every different functions. In the current case, where no specific information is known regarding the function, it is entirely unpredictable what function and activity will

be found for the protein. The prior art does not resolve this ambiguity, since no prior art activity is identified for the encoded polypeptides.

The amount of direction or guidance presented and the existence of working examples.

The specification discloses only a polynucleotide of SEQ ID NO:271 encoding a polypeptide having MDH activity or the full complement of SEQ ID NO:271, vector comprising said polynucleotide, and a plant cell comprising said vector. However, the speciation fails to provide any information as to (1) specific substrates associated with the MDH encoded by SEQ ID NO:271, (2) structural elements required in a polypeptide having MDH activity, or (3) which are the structural elements in MDH or the polypeptide encode by SEQ ID NO:271 that are essential to MDH activity. No correlation between structure and function of having MDH activity has been presented. There is no information or guidance as to which amino acid residues in the polypeptides encoded by SEQ ID NO:271 can be modified and which ones are to be conserved to create a polypeptide displaying the same activity as that of the polypeptides of SEQ ID NO:271.

Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability of the prior art in regard to structural changes and their effect on function and the lack of knowledge about a correlation between structure and function, an undue experimentation would be necessary one having ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of

enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides having the desired biological characteristics recited in the claim are unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicants argue that the claims meet the enablement requirement because amendment of the claims overcomes the rejection and the functional activity is MDH activity. Examiner respectfully disagrees. Regarding claim 33, examiner has broadly interpreted "functionally active" to encompass polypeptides having any function (see the rejection of the phrase "functionally active" under 35 USC 112, 2nd paragraph). Examiner has broadly interpreted claims 31, 33, 35, and 40-42 to encompass to **(A)** polynucleotide encoding (1) MDH isolated from any or all *Trifolium* sources, including any or all variants, mutants, or recombinants thereof; **(B)** a polynucleotide encoding MDH from white clover (*T. repens*), including any or all any variants, mutants, or recombinants of; **(C)** any or all polynucleotides having at least 95% sequence identity to SEQ ID NO:271 and encoding polypeptides having unknown function; and **(D)** construct comprising said polynucleotide of (A), (B), or (C), and plant cell comprising said construct. Therefore, the claims are drawn to polynucleotides having unknown structure and/or unknown function. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides of virtually any structure and/or function or polypeptides/variants having virtually any structure and/or function. The specification only disclose cDNA encoding

a malate dehydrogenase from *Trifolium repens* and a cDNA encoding a malate dehydrogenase from *Lolium perenne*. As discussed above, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a specific knowledge of and guidance with regard to which specific amino acids in the protein's sequence, can be modified such that the modified polypeptide continues to have said claimed activity. It is this specific guidance that applicants do not provide. While the art may teach in general the structure of EGIII conserved amino acid sequences, X-ray crystal structure and etc, such teachings will not reduce the burden of undue experimentation on those of ordinary skill in the art.

Hence the rejection is **maintained.**

Claim Rejections - 35 USC § 102

In view of the amendment of claim 30, which is now limited to a polynucleotide to that isolated from *Trifolium*, the rejection of claims 30, 33, 35, and 40-42 under 35 U.S.C. 102(b) as being anticipated by Tesfaye et al. has been **withdrawn**.

In view of the amendment of claim 30, deletion of the phrase "MDH-like", the rejection of claims 30, 31, 33, and 35 U.S.C. 102(b) as being anticipated by Ellison et al. has been **withdrawn**.

Conclusion

Claims 30-31, 33, 35, 40-42, 58-63 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Yong D Pak/
Primary Examiner, Art Unit 1652